

Analysis of HIF-1 alpha and HIF-2 alpha in dendritic cells stimulated under hypoxic conditions

Barroeta Seijas AB.¹, Filippi I.², Vitale S.¹, Simonetti S.³, Naldini A.², Di Rosa F.¹

¹ Institute of Biology and Molecular Pathology (IBPM)- National Research Council (CNR), Rome, Italy

² Department of Physiology, University of Siena, Siena, Italy.

³ Department of Molecular Medicine, University of Rome "Sapienza", Rome, Italy

Dendritic cells (DCs) are professional antigen-presenting cells that have a pivotal role in linking innate and acquired immunity, and in the maintenance of self-tolerance. DCs can activate resting T cells in spleen and lymph nodes, stimulate effector T cells in inflamed tissues and contribute to maintenance of memory T cells in different organs, including the bone marrow (BM). Alternatively activated DCs have been involved in regulation of angiogenesis during chronic inflammation. Inflamed tissues and BM share a common feature: a low oxygen tension. Under hypoxic conditions, different levels of hypoxia inducible factors HIF-1 alpha and HIF-2 alpha modulate the expression of a variety of genes related to apoptosis, cell migration, metabolic changes necessary for adaptation to the hypoxic environment. Although it is generally believed that hypoxic conditions are inhibitory for protective immune responses, a clear picture of the hypoxia-induced pathways in DCs has not emerged yet.

We aim to investigate the molecular and functional changes induced by hypoxia in mouse BM-derived DCs. Specifically, we will evaluate the regulation of the transcription factors HIF-1 alpha and HIF-2 alpha in DCs stimulated with classical (e.g. LPS) and alternative stimuli (e.g. IL-10), under either normoxic or hypoxic conditions. We will investigate the production by stimulated DCs of molecular mediators affecting both angiogenesis and T cell responses. We expect to gain more information on the cross-talk between angiogenic molecules and cytokines involved in immune regulation, occurring both in hypoxic lymphoid organs and inflamed tissues.